TXR NO. 0050466

February 12, 2002

MEMORANDUM

SUBJECT: ***TEBUTHIURON***- Report of the FQPA Safety Factor Committee.

FROM: Carol Christensen, Acting Executive Secretary
FQPA Safety Factor Committee
Health Effects Division (7509C)

THROUGH: Ed Zager, Chairman
FQPA Safety Factor Committee
Health Effects Division (7509C)

TO: Paula Deschamp, Risk Assessor
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Health Effects Division (7509C)

PC Code: 105501

The Health Effects Division (HED) FQPA Safety Factor Committee met on February 4th , 2002 to evaluate the hazard and exposure data for tebuthiuron. The Committee recommend that the FQPA Safety Factor (as required by the FQPA) be reduced to **3x** when assessing the exposure and risks of this chemical to human health.

I. HAZARD ASSESSMENT

(Correspondence: R. Fricke to C. Christensen dated January 31, 2002)

A. Adequacy of Database

The Hazard Identification Assessment Review Committee (HIARC) met on December 13th, 2001 and on January 7th, 2002 to review the toxicological database of tebuthiuron. The toxicological database is adequate for FQPA assessment, however there are significant data gaps. The developmental toxicity study in the rabbit is unacceptable for the determination of susceptibility to the fetuses due to *in utero* tebuthiuron exposure. However, there is an adequate developmental toxicity study in the rat and a two-generation reproductive toxicity study in the rat to assess the susceptibility of fetuses/off-spring to tebuthiuron. The Committee reserved the requirement of a developmental neurotoxicity study due to the data gap for a developmental toxicity study in rabbits.

B. Determination of Susceptibility

There is no qualitative/quantitative evidence of increased susceptibility in the 2-generation reproduction study in the rat or the developmental toxicity study in the rat. In the developmental toxicity study in the rabbit, no maternal or developmental toxicity was observed at the highest dose tested. Because there was no toxicity observed at the highest dose tested, susceptibility could not be ascertainted and the HIARC concluded that a new developmental toxicity in the rabbit is needed.

II. EXPOSURE ASSESSMENT

(*Correspondence: S. Piper to C. Christensen dated January 31, 2002)*

A. Dietary Exposure Considerations

Tebuthiuron is an herbicide registered for use on pastures and rangeland. The chemical is registered for a single broadcast application to rangeland and forage grasses by ground or air equipment with an application rate of 0.75-4.00 lb ai/A. The recommended timing of application is prior to the resumption of active seasonal growth in the spring or before expected seasonal rainfall. Tolerances range from 0.8-5.0 ppm for secondary residues and 10 ppm for forage. There are no Codex MRLs established or proposed for residues of tebuthiuron. Therefore, issues of compatibility with respect to U.S. tolerances and Codex MRLs do not exist.

The qualitative nature of the residue in grasses is adequately understood. The residues of concern are the parent compound and its metabolites 103(OH), 104, and 109. The terminal residues of concern in fat, meat, kidney, and liver are tebuthiuron and its metabolites 104, 106, 108 and 109; the terminal residues of concern in milk are

tebuthiuron and metabolites 104, 104(OH), 106, 109 and 109(OH). Tebuthiuron is a systemic soil herbicide that is absorbed mainly by the roots, with ready translocation.

There are no monitoring data (PDP or FDA) for Tebuthiuron. Percent of crop treated information is available for use in the assessment. A DEEM Tier II analysis will likely be used to assess dietary exposure to this chemical using the results of field trial studies and percent of crop treated data.

The Committee recognizes that further refinement to the dietary food exposure analyses may be required as the risk assessment is developed. Therefore, provided the final dietary food exposure assessment includes the metabolites of toxicological concern and does not underestimate the potential risk for infants and children, the safety factor recommendations of this Committee stand.

B. Drinking Water Exposure Considerations

The environmental fate database is essentially complete for parent tebuthiuron. Tebuthiuron water degradate 104 was detected at 6.9% and rising by the end of the study. The HED Metabolism Assessment and Review Committee (MARC) recommended degradate 104 be included in the water exposure and risk assessment. Based on the available data, the parent and degradate 104 are persistent and mobile. The quickest observed route of tebuthiuron degradation in laboratory studies was soil photolysis (half-life 39.7 days.)

Tebuthiuron has been assessed through a combination of modeling and analysis of surface water and ground water monitoring data. Drinking-water monitoring results are not available for the chemical for direct quantitative incorporation into the exposure and risk assessment. Therefore, drinking water exposure assessments are supplemented with modeling predictions. Surface water concentrations of tebuthiuron were modeled using the PRZM/EXAMS (Tier II) programs for pasture/rangeland using EFED's standard scenario for alfalfa in Texas. Groundwater concentrations were modeled using the SCI-GROW program. Input parameters used Tier II (PRZM version 3.12/EXAMS version 2.97.5) modeling were selecting using Agency guidance and EFED calculated degradation rate constants from review of registrant submitted environmental fate studies. This assessment strategy was designed to assess concentrations of the parent compound.

In order to account for the degradate of toxicological concern, EFED will complete modeling of the degradate using the total residue approach. Total residues (parent plus all degradates of toxicological concern) are summed from fate studies. In this case fate parameters are estimated for total residues for aerobic soil metabolism, aerobic aquatic metabolism, anaerobic soil metabolism, and photolysis. Other required fate parameters are conservatively estimated as stable in accordance with EFED guidance. This method

provides conservative estimates of total residues (parent plus degradates) in surface and ground water. Drinking water monitoring data support the results of the drinking water models.

The FQPA Safety Factor Committee recognizes that further refinement to the dietary water exposure analyses may be required as the risk assessment is developed. Therefore, provided the final dietary water exposure assessment includes the metabolite of toxicological concern and does not underestimate the potential risk for infants and children, the safety factor recommendations of this Committee stand.

C. Residential Exposure Considerations

There are no registered residential uses for tebuthiuron.

III. RISK CHARACTERIZATION

A. FQPA Safety Factor Recommendation

The Committee recommended that the FQPA Safety factor for enhanced sensitivity to infants and children (as required by FQPA) should be **reduced (3x).**

A. Rationale for Reducing the FQPA Safety Factor

The Committee concluded that the safety factor could be reduced for Tebuthiuron because:

1. There is no indication of quantitative or qualitative increased susceptibility of rats to *in utero* exposure;
2. There is no indication of quantitative or qualitative increased susceptibility of rat offspring seen in the two-generation reproductive toxicity study;
3. The dietary (food and drinking water) exposure assessments will not underestimate the potential exposures for infants and children.

However, the Committee decided that a factor is needed **(3x)** because of the data gap for a developmental toxicity study in the rabbit.

C. Application of the FQPA Safety Factor:

Acute Dietary Exposure (Females 13-50): When assessing acute dietary exposure to females 13-50, the reduced FQPA safety factor of **3x** will be used. This is because there is a data gap for assessing susceptibility of fetuses following *in utero* exposure to tebuthiuron.

Chronic Dietary Exposure (General Population): When assessing chronic dietary exposure to the general population, the FQPA safety factor will be removed **(1x)**. This is because there was no susceptibility identified in the 2-generation rat reproduction study (a long-term study).